

FIG. 1

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GenBank accession number: F01481.1

FIG. 2

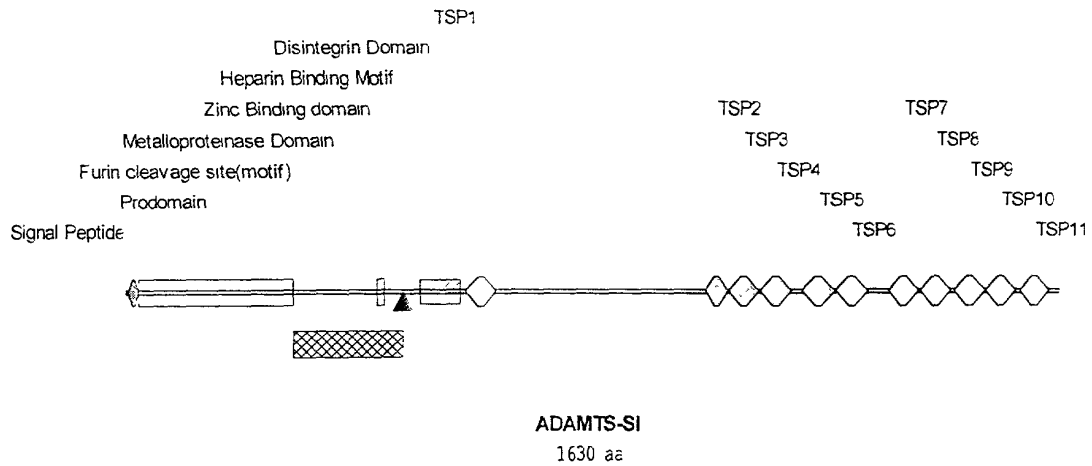
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wel*
25

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10
15
20
25

Fig. 3

Domain structure of ADAMTS-SI

Signal peptide (1-18), Prodomain (19-287), Furin cleavage site (288), Metalloproteinase domain (289-478), Zinc binding motif (434-446), Heparin binding motif (478-482), Disintegrin domain (509-578), Thrombospondin motif (589-642), Spacer region (643-1014), Thrombospondin submotifs (1001-1053, 1056-1108, 1111-1165, 1186-1239, 1240-1295, 1332-1383, 1386-1439, 1445-1500, 1501-1554, 1559-1612)



B

1 CCGGAATTCC CGGGTCGACC CACGCGTCCG GCCCCCCATT CAAGAAGCCG CTCAGCTATC
 GGCCTTAAGG GCCCAGCTGG GTGCGCAGGC CGGGGGGTAA GTTCTTCGGC GAGTCGATAG

61 CCGGCCAGCA CAGGGCGCCC GCGCGCCTC GGAGCGCAAG TTCCTCGCCT TCTCTGCC
 GGCCGGTCGT GTCCCGCGG CCGCGCGGAG CCTCGCGTTC AAGGAGCGGA AGAGGACGGG

121 GCTCGCTGGG CATTATGCGG CCAAGCAGCC GAGCCCCAGT CCTCCTCCTC CTCTGTCTCC
 CGAGCGACCC GTAATACGCC GGTTCGTCGG CTCGGGTCA GGAGGAGGAG GAGGACGAGG

181 TCCGGTCTCT CCTGCGGCC GAGCGGCTCA GCTCTCGGCA GGCGGCGGCG TTGCTCAGCC
 AGGCCGAGGA GGACGCCGG CTCGCCGAGT CGAGAGCCGT CCGCCGCCGC AACGAGTCGG

241 GAGCGCAGAC GGGACCCTCG CAGCGAGACC TCAGCGACTC CTAAGTCAA AAGTTGGCGG
 CTCGCGTCTG CCCTGGGAGC GTCGCTCTGG AGTCGCTGAG GATTTCAGTT TTCAACCGCC

301 CGGGCGCGG GCTCCGCGG CTCTCCACGG CCGTGCCTC GCGTCGCCG CGCAGCCAAG
 GCGCGCGCC CGAGGCGCG GAGAGGTGCC GCGACGGAG CGCAGCGGCG GCGTCGGTTC

+2 M Q F
 Start met
 ===
 Kozak consensus
 =====
 Signal peptide
 =====

361 GAGGGCAGGA GGGAGGGGG TGGGGCAGC GGAGGGAGG GTGGGAAGCA CCATGCAGTT
 CTCCTGCTCT CCCTCCCCC ACCCCCGTCC CCTCCCTCCC CACCCTTCGT GGTACGTCAA

+2 V S W A T L L T L L V R D L A E M G S P
 signal peptide cleavage site

Signal peptide Prodomain

421 TGTATCCTGG GCCACACTGC TAACGCTCCT GGTGCGGGAC CTGGCCGAGA TGGGAGGCC
 ACATAGGACC CGGTGTGACG ATTGCGAGGA CCACGCCCTG GACCGGCTCT ACCCCTCGGG

+2 D A A A A V R K D R L H P R Q V K L L E
 Prodomain

481 AGACGCCGCG GCGGCCGTGC GCAAGGACAG GCTGCACCCG AGGCAAGTGA AATTATTAGA
 TCTGCGGCGC CGCCGGCAGC CGTTCCTGTC CGACGTGGGC TCCGTCACT TTAATAATCT

+2 T L S E Y E I V S P I R V N A L G E P F
 Prodomain

541 GACCCTGAGC GAATACGAAA TCGTGTCTCC CATCCGAGTG AACGCTCTCG GAGAACCCTT
 CTGGGACTCG CTTATGCTTT AGCACAGAGG GTAGGCTCAC TTGCGAGAGC CTCTTGGGAA

+2 P T N V H F K R T R R S I N S A T D P W
 Prodomain

601 TCCCACGAAC GTCCACTTCA AAAGAACGCG ACGGAGCATT AACTCTGCCA CTGACCCCTG

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

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+2 P A F A S S S S S S T S S Q A H Y R L S
                                         Prodomain
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661 GCCTGCCTTC GCCTCCTCCT CTCCTCCTC TACCTCCTCC CAGGGGCATT ACCGCCTCTC
    CGGACGGAAG CGGAGGAGGA GAAGGAGGAG ATGGAGGAGG GTCCGCGTAA TGGCGGAGAG

+2 A F G Q Q F L F N L T A N A G F I A P I
                                         Prodomain
=====
721 TGCCTTCGGC CAGCAGTTC TATTTAATCT CACCGCCAAT GCCGGATTTA TCGCTCCACT
    ACGGAAGCCG GTCGTCAAAG ATAAATTAGA GTGGCGGTTA CGGCCTAAAT AGCGAGGTGA

+2 F T V T L L G T P G V N Q T K F Y S E E
                                         Prodomain
=====
781 GTTCACTGTC ACCCTCCTCG GGACGCCCGG GGTGAATCAG ACCAAGTTTT ATTCCGAAGA
    CAAGTGACAG TGGGAGGAGC CCTGCGGGCC CCACTTAGTC TGGTTCAAAA TAAGGCTTCT

+2 E A E L K H C F Y K G Y V N T N S E H T
                                         Prodomain
=====
841 GGAAGCGGAA CTCAGCACT GTTCTACAA AGGCTATGTC AATACCAACT CCGAGCACAC
    CCTTCGCCCTT GAGTTCGTA CAAAGATGTT TCCGATACAG TTATGGTTGA GGCTCGTGTG

+2 A V I S L C S G M L G T F R S H D G D Y
    Prodomain
=====
901 GGCCGTCATC AGCCTCTGCT CAGGAATGCT GGGCACATTC CGGTCTCATG ATGGGGATTA
    CCGGCAGTAG TCGGAGACGA GTCCTTACGA CCCGTGTAAG GCCAGAGTAC TACCCCTAAT

+2 F I E P L Q S M D E Q E D E E E Q N K P
    Prodomain
=====
961 TTTTATTGAA CCACTACAGT CTATGGATGA ACAAGAAGAT GAAGAGGAAC AAAACAAACC
    AAAATAACTT GGTGATGTC AATACTACT TGTCTTCTA CTTCTCCTTG TTTTGTGG

+2 H I I Y R R S A P Q R E P S T G R H A C
    Prodomain
=====
1021 CCACATCATT TATAGGCGCA GCGCCCCCA GAGAGAGCCC TCAACAGGAA GGCATGCATG
    GGTGTAGTAA ATATCCGCGT CGCGGGGGT CTCTCTCGGG AGTTGTCCTT CCGTACGTAC

+2 D T S E H K N R H S K D K K K T R A R K
    Prodomain
=====
1081 TGACACCTCA GAACACAAA ATAGGCACAG TAAAGACAAG AAGAAAACCA GAGCAAGAAA
    ACTIGTGAGT CTGTGTGTTT TATCCGTGTC ATTTCTGTTC TTCTTTGGT CTCGTTCTTT

+2 W G E R I N L A G D V A A L N S G L A T
    Prodomain
=====
1141 ATGGGGAGAA AGGATTAACC TGGCTGGTGA CGTAGCAGCA TTAACAGCG GCTTAGCAAC
    TACCCCTCTT TCCTAATTGG ACGACCACT GCATCGTCGT AATTGTGCG CGAATCGTTG

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1141 ATGGGGAGAA AGGATTAACC TGGCTGGTGA CGTAGCAGCA TTAACAGCG GCTTAGCAAC

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-2  E A F S A Y G N K T D N T R E K R T H F
    Prodomain.
=====
1201 AGAGGCATTT TCTGCTTATG GTAATAAGAC GGACAACACA AGAGAAAAGA GGACCCACAG
    TCTCCGTAAA AGACGAATAC CATTATTCTG CCTGTGTGTG TCTCTTTTCT CCTGGGTGTC

+2  R T K R F L S Y P R F V E V L V V A D N
    Furin Cleavage site

    Prodomain.                               Metalloproteinase domain
=====
1261 AAGGACAAAA CGTTTTTAT CCTATCCACG GTTTGTAGAA GTCTTGGTGG TGGCAGACAA
    TTCTTGTTTT GCAAAAAATA GGATAGGTGC CAAACATCTT CAGAACCACC ACCGTCTGTT

+2  R M V S Y H G E N L Q H Y I L T L M S I
    Metalloproteinase domain
=====
1321 CAGAATGGTT TCATACCATG GAGAAAACCT TCAACACTAT ATTTAACTT TAATGTCAAT
    GTCTTACCAA AGTATGGTAC CTCTTTTGA AGTTGTGATA TAAAATTGAA ATTACAGTTA

+2  V A S I Y K D P S I G N L I N I V I V N
    Metalloproteinase domain
=====
1381 TGTAGCCTCT ATCTATAAAG ACCCAAGTAT TGGAAATTTA ATTAATATTG TTATTGTGAA
    ACATCGGAGA TAGATATTTC TGGGTTTATA ACCTTTAAAT TAATTATAAC AATAACACTT

+2  L I V I H N E Q D G P S I S F N A Q T T
    Metalloproteinase domain
=====
1441 CTTAATGTG ATTATAATG AACAGGATGG GCCTTCCATA TCTTTTAATG CTCAGACAAC
    GAATTAACAC TAAGTATTAC TTGTCCTACC CGGAAGGTAT AGAAAATTAC GAGTCTGTTG

+2  L K N F C Q W Q H S K N S P G G I H H D
    Metalloproteinase domain
=====
1501 ATTAATAAAC TTTTGCCAGT GGCAGCATTG GAAGAACAGT CCAGGTGGAA TCCATCATGA
    TAATTTTTTG AAAACGGTCA CCGTCGTAAG CTCTTGTCA GGTCCACCTT AGGTAGTACT

+2  T A V L L T R Q D I C R A H D K C D T I
    Metalloproteinase domain
=====
1561 TACTGCTGTT CTCTTAACAA GACAGGATAT CTGCAGAGCT CACGACAAAT GTGATACCTT
    ATGACGACAA GAGAATTGTT CTGTCCTATA GACGTCTCGA GTGCTGTGTTA CACTATGGAA

+2  G L A E L G T I C D P Y R S C S I S E I
    Metalloproteinase domain
=====
1621 AGGCCTGGCT GAACTGGGAA CCATTTGTGA TCCCTATAGA AGCTGTTCTA TTAGTGAAGA
    TCCGGACCGA CTTGACCCTT GGTAAACACT AGGGATATCT TCGACAAGAT AATCACTTCT

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P... ..

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+2  S G L S T A F T I A H E L G H V F N M F
                                     Zinc Binding Domain
=====
Metalloproteinase domain.
=====
1681 TAGTGGATTG AGTACAGCTT TTACGATCGC CCAIGAGCTG GGCCATGTGT TTAACATGCC
    ATCACCTAAC TCATGTCGAA AATGCTAGCG GGTACTCGAC CCGGTACACA AATTGTACGG

+2  H D D N N K C K E E G V K S P Q H V M A
    Zinc Binding Domain
=====
Metalloproteinase domain.
=====
1741 TCATGATGAC AACACAAAT GTAAAGAAGA AGGAGTTAAG AGTCCCAGC ATGTCATGGC
    AGTACTACTG TTGTGTTTA CATTCTTCT TCCTCAATTC TCAGGGGTCG TACAGTACCG

+2  P T L N F Y T N P W M W S K C S R K Y I
                                     Heparin Binding Motif
=====
Metalloproteinase domain.                               Heparin Binding Motif
=====
1801 TCCAACACTG AACTTCTACA CCAACCCCTG GATGTGGTCA AAGTGTAGTC GAAAATATAT
    AGGTTGTGAC TTGAAGATGT GGTGTTGGGAC CTACACCAGT TTCACATCAG CTTTTATATA

+2  T E F L D T G Y G E C L L N E P E S R P
1861 CACTGAGTTT TTAGACACTG GTTATGGCGA GTGTTTGCTT AACGAACCTG AATCCAGACC
    GTGACTCAA AATCTGTGAC CAATACCGCT CACAAACGAA TTGCTTGGAC TTAGGTCTGG

+2  Y P L P V Q L P G I L Y N V N K Q C E L
                                     Disintegrin domain
=====
1921 CTACCCTTTG CCTGTCCAAC TCCAGGCAT CCTTTACAAC GTGAATAAAC AATGTGAATT
    GATGGGAAAC GGACAGGTTG ACGGTCCGTA GGAAATGTTG CACTTATTTG TTACACTTAA

+2  I F G P G S Q V C P Y M M Q C R R L W C
                                     Disintegrin domain
=====
1981 GATTTTGGGA CCAGGTTCTC AGGTGTGCC ATATATGATG CAGTGCAGAC GGCTCTGGTG
    CTA AAAACCT GGTCCAAGAG TCCACACGGG TATATACTAC GTCACGTCTG CCGAGACCAC

+2  N N V N G V H K G C R T Q H T P W A D G
                                     Disintegrin domain.
=====
2041 CAATAACGTC AATGGAGTAC ACAAAGGCTG CCGGACTCAG CACACACCCT GGGCCGATGG
    GTTATTGCAG TTACCTCATG TGTTCGAC GGCCTGAGTC GTGTGTGGGA CCCGGCTACC

+2  T E C E P G K H C K Y G F C V P K E M D
    Disintegrin domain
=====
2101 GACGGAGTGC GAGCCTGGAA AGCACTGCAA GTATGGATTT TGTGTTCCCA AAGAAATGGA
    CTGCCTCAG CTCGGACCTT TCGTGACGTT CATACCTAAA ACACAAGGGT TTCTTTACCT

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V P V T D G S W G S W S F F G T C S R T
Disintegrin domain TSP1
=====
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ACAGGGGCAC TGTCTACCTA GGACCCCTTC AACCTCAGGG AAACCTTGGA CGAGGTCTTG

+2 C G G G I K T A I R E C N R P E P K N G
TSP1
=====
2221 ATGTGGAGGG GGCATCAAAA CAGCCATTCC AGAGTGCAAC AGACCAGAAC CAAAAAATGG
TACACCTCCC CCGTAGTTTT GTCGTAAGC TCTCACGTTG TCTGGTCTTG GTTTTTTACC

+2 G K Y C V G R R M K F K S C N T E P C L
TSP1 Spacer Region
=====
2281 TGGAAAATAC TGTGTAGGAC GTAGAATGAA ATTTAAGTCC TGCAACACGG AGCCATGTCT
ACCTTTTATG ACACATCTCG CATCTTACTT TAAATTCAGG ACGTTGTGCC TCGGTACAGA

+2 K Q K R D F R D E Q C A H F D G K H F N
Spacer Region
=====
2341 CAAGCAGAAG CGAGACTICC GAGATGAACA GTGTGCTCAC TTTGACGGGA AGCATTTTAA
GTTCGTCTTC GCTCTGAAGG CTCTACTTGT CACACGAGTG AAACCTGCCCT TCGTAAAATT

+2 I N G L L P N V R W V P K Y S G I L M K
Spacer Region
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2401 CATCAACGGT CTGCTTCCCA ATGTGCGCTG GGTCCTTAAA TACAGTGGAA TTCTGATGAA
GTAGTTGCCA GACGAAGGGT TACACGCGAC CCAGGGATTT ATGTCACCTT AAGACTACTT

+2 D R C K L F C R V A G N T A Y Y Q L R D
Spacer Region
=====
2461 GGACCGGTGC AAGTIGTICT GCAGAGTGGC AGGGAACACA GCCTACTATC AGCTTCGAGA
CCTGGCCACG TTCAACAAGA CGTCTACCG TCCCTTGTGT CGGATGATAG ICGAAGCTCT

+2 R V I D G T F C G Q D T N D I C V Q G L
Spacer Region
=====
2521 CAGAGTGATA GATGGAATC CTGTGGCCA GGACACAAAT GATATCTGTG TCCAGGGCCT
GTCTCACTAT CTACCTTGAG GAACACCGGT CCTGTGTTTA CTATAGACAC AGGTCCCGGA

+2 C R Q A G C D H V L N S K A R R D K C G
Spacer Region
=====
2581 TTGCCGGCAA GCTGATGCG ATCATGTTTT AAACCAAAA GCCCGGAGAG ATAAATGTGG
AACGGCCGTT CGACCTACGC TAGTACAAAA TTTGAGTTTT CGGGCCTCTC TATTACACC

+2 V C G G D N S S C K T V A G T F N T V H
Spacer Region
=====
2641 GGTITGTGGT GGCATAATT CTTGATGCAA AACAGTGGCA GGAACATTTA ATACAGTACA
CCAAACACCA CCGCTATTAA GAAGTACGTT TTGTCACCGT CCTTGTAAT TATGTCATGT

```

The following sequence is a partial sequence of the protein.

+2 Y G Y N T V V R I F A G A T N I D V R Q
Spacer Region.

=====
2701 TTATGGTTAC AATACTGTGG TCCGAATTCC AGCTGGTGCT ACCAATATTG ATGTGCGGCA
AATACCAATG TTATGACACC AGGCTTAAGG TCGACCACGA TGGTTATAAC TACACGCCGT

+2 H S F S G E T D D D N Y L A L S S S K G
Spacer Region.

=====
2761 GCACAGTTTC TCAGGGGAAA CAGACGATGA CAACTACTTA GCTTTATCAA GCAGTAAAGG
CGTGTCAAAG AGTCCCCTTT GTCTGCTACT GTTGATGAAT CGAAATAGTT CGTCATTTCC

+2 E F L L N G N F V V T M A K R E I R I G
Spacer Region.

=====
2821 TGAATCTTG CTAATGGAA ACTTTGTTGT CACAATGGCC AAAAGGGAAA TTCGCATTGG
ACTTAAGAAC GATTTACCTT TGAACAACA GTGTTACCGG TTTCCCTTT AAGCGTAACC

+2 N A V V E Y S G S E T A V E R I N S T D
Spacer Region

=====
2881 GAATGCTGTG GTAGAGTACA GTGGGTCCGA GACTGCCGTA GAAAGAATTA ACTCAACAGA
CTTAGACAC CATCTCATGT CACCCAGGCT CTGACGGCAT CTTTCTTAAT TGAGTTGTCT

+2 R I E Q E L L L Q V L S V G K L Y N P E
Spacer Region

=====
2941 TCGCATTGAG CAAGAACCTT TGCTTCAGGT TTTGTGGTG GAAAGTTGT ACAACCCCGA
AGCGTAACCT GTTCTTGAAA ACGAAGTCCA AAACAGCCAC CCTTCAACA TGTTGGGGCT

+2 V R Y S F N I P I E D K P Q Q F Y W N S
Spacer Region

=====
3001 TGTACGCTAT TCTTCAATA TTCCAATTGA AGATAAACCT CAGCAGTTTT ACTGGAACAG
ACATGCGATA AGAAAGTTAT AAGGTAACT TCTATTGGA GTCGTCAAAA TGACCTTGTC

+2 H G P W Q A C S K P C Q G E R K R K L V
Spacer Region

=====
3061 TCATGGGCCA TGGCAAGCAT GCAGTAAACC CTGCCAAGGG GAACGGAAAC GAAAACCTGT
AGTACCCGGT ACCGTTTCGTA CGTCATTGG GACGGTCCCT CTTGCCTTG CTTTGAACA

+2 C T R E S D Q L T V S D Q R C D R L P C
Spacer Region

=====
3121 TTGCACCAGG GAATCTGATC AGCTTACTGT TTCTGATCAA AGATGCGATC GGCTGCCCCA
AACGTGGTCC CTTAGACTAG TCGAATGACA AAGACTAGTT TCTACGCTAG CCGACGGGGT

+2 P G H I T E P C G T D C D L R W H V A S
Spacer Region

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3181 GCCTGGACAC ATTACTGAAC CCTGTGGTAC AGACTGTGAC CTGAGGTGGC ATGTTGCCAG
CGGACCTGTG TAATGACTTG GGACACCATG TCTGACTG GACTCCACCG TACAACGGTC

3181 GCCTGGACAC ATTACTGAAC CCTGTGGTAC AGACTGTGAC CTGAGGTGGC ATGTTGCCAG
CGGACCTGTG TAATGACTTG GGACACCATG TCTGACTG GACTCCACCG TACAACGGTC

+2 R S E C S A Q C G L G Y R T L D I Y C A
Spacer Region

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3241 CAGGAGTGAA TGTAGTGGCC AGTGTGGCTT GGGTTACCGC ACATTGGACA TCTACTGTGC
GTCCTCACTT ACATCACGGG TCACACCGAA CCCAATGGCG TGTAACCTGT AGATGACACG

+2 K Y S R L D G K T E K V D D G F C S S H
Spacer Region

=====
3301 CAAATATAGC AGGCTGGATG GGAAGACTGA GAAGGTTGAT GATGGTTTTT GCAGCAGCCA
GTTTATATCG TCCGACCTAC CCTTCTGACT CTTCCAAC TAACCAAAAA CGTCGTCGGT

+2 P K F S N R E K C S G E C N T G G W R Y
Spacer Region

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3361 TCCCAAACCA AGCAACCGTG AAAAAAGCTC AGGGGAATGT AACACGGGTG GCTGGCGCTA
AGGGTTTGGT TCGTTGGCAC TTTTACGAG TCCCCTTACA TTGTGCCAC CGACCGCGAT

+2 S A W T E C S K S C D G G T Q R R R A I
Spacer Region TSP2

=====
3421 TTCTGCTGG ACTGAATGTT CAAAAGCTG TGACGGTGGG ACCCAGAGGA GAAGGGCTAT
AAGACGGACC TGACTTACAA GTTTTCGAC ACTGCCACCC TGGGTCTCCT CTCCCGATA

+2 C V N T R N D V L D D S K C T H Q E K V
TSP2

=====
3481 TTGTGTCAAT ACCCGAAATG ATGTACTGGA TGACAGCAA TGCACACATC AAGAGAAAGT
AACACAGTTA TGGGCTTTAC TACATGACCT ACTGTCGTTT ACGTGTGTAG TTCTCTTTCA

+2 T I Q R C S E F P C P Q W K S G D W S E
TSP2 TSP3

=====
3541 TACCATTAG AGGTGCAGTG AGTTCCCTTG TCCACAGTGG AAATCTGGAG ACTGGTCAGA
ATGTTAAGTC TCCACGTCAC TCAAGGGAAC AGGTGTCACC TTTAGACCTC TGACCAGTCT

+2 C L V T C G K G H K H R Q V W C Q F G E
TSP3

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3601 GTGCTTGGTC ACCTGTGGAA AAGGGCATAA GCACCGCCAG GTCTGGTGTG AGTTTGGTGA
CACGAACCAG TGGACACCTT TTCCCGTATT CGTGGCGGTC CAGACCACAG TCAAACCACT

+2 D R L N D R M C D F E T K P T S M Q T C
TSP3

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3661 AGATCGATTA AATGATAGAA TGTGTGACCC TGAGACCAAG CCAACATCTA TGCAGACTTG
TCTAGCTAAT TTAATATCTT ACACACTGGG ACTCTGGTTC GGTGTAGAT ACGTCTGAAC

+2 Q Q P E C A S W Q A G P W G Q C S V T C
TSP3 TSP4

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3721 TCAGCAGCCG GAATGTGCAT CCTGGCAGGC GGGTCCCTGG GGACAGTGCA GTGTCACTTG
AGTCGTCGGC CTTACACGTA GGACCGTCCG CCCAGGGACC CCTGTACAGT CACAGTGAAC

3721 TCAGCAGCCG GAATGTGCAT CCTGGCAGGC GGGTCCCTGG GGACAGTGCA GTGTCACTTG
AGTCGTCGGC CTTACACGTA GGACCGTCCG CCCAGGGACC CCTGTACAGT CACAGTGAAC

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+2      G Q G Y Q L R A V K C I I G T Y M S V V
          TSP4
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3781  TGGACAGGGA TACCAGCTAA GAGCAGTGAA ATGCATCATT GGGACTTATA TGTCAGTGGT
      ACCTGTCCCT ATGGTCGATT CTCGTCACCT TACGTAGTAA CCCTGAATAT ACAGTCACCA

+2      D D N D C N A A T R P T D T Q D C E L F
          TSP4
=====
3841  AGATGACAAT GACTGTAATG CAGCAACTAG ACCCACTGAT ACCCAGGACT GTGAATTACC
      TCTACTGTTA CTGACATTAC GTCGTTGATC TGGTTGACTA TGGGTCCTGA CACTTAATGG

+2      S C H P P P A A P E T R R S T Y S A P R
          TSP4
=====
3901  ATCATGTTCAT CCTCCCCCAG CTGCCCCGGA AACGAGGAGA AGCACATACA GTGCACCAAG
      TAGTACAGTA GGAGGGGGTC GACGGGGCCT TTGCTCCTCT TCGTGTATGT CACGTGGTTC

+2      T Q W R F G S W T P C S A T C G K G T R
          TSP5
=====
3961  AACCCAGTGG CGATTGGGT CTGGACCCC ATGCTCAGCC ACTTGTGGGA AAGGTACCCG
      TTGGGTCACC GCTAAACCCA GAACCTGGGG TACGAGTCGG TGAACACCCT TTCCATGGGC

+2      M R Y V S C R D E N G S V A D E S A C A
          TSP5
=====
4021  GATGAGATAC GTCAGCTGCC GAGATGAGAA TGGCTCTGTG GCTGACGAGA GTGCCTGTGC
      CTACTCTATG CAGTCGACGG CTCTACTCTT ACCGAGACAC CGACTGCTCT CACGGACACG

+2      T L P R P V A K E E C S V T P C G Q W K
          TSP5 TSP6
=====
4081  TACCTGCCT AGACCAAGTGG CAAAGGAAGA ATGTTCTGTG ACACCTGTG GGCAATGGAA
      ATGGGACGGA TCTGGTCACC GTTTCCTTCT TACAAGACAC TGTGGGACAC CCGTACCTT

+2      A L D W S S C S V T C G Q G R A T R Q V
          TSP6
=====
4141  GGCCTGGAC TGGAGCTCTT GCTCTGTGAC CTGTGGGCAA GGTAGGGCAA CCCGGCAAGT
      CCGGAACCTG ACCTCGAGAA CGAGACACTG GACACCCGTT CCATCCCGTT GGGCCGTTCA

+2      M C V N Y S D H V I D R S E C D Q D Y I
          TSP6
=====
4201  GATGTGTGTC AACTACAGTG ACCACGTGAT CGATCGGAGT GAGTGTGACC AGGATTATAT
      CTACACACAG TTGATGTAC TGGTGCACTA GCTAGCCTCA CTCACACTGG TCCTAATATA

+2      P E T D Q D C S M S P C P Q R T P D S G
          TSP6
=====
4261  CCCGAAACT GACCAGGACT GTTCCATGTC ACCATGCCCT CAAAGGACCC CAGACAGTGG
      GGGTCTTGA CTGGTCTGA CAAGGTACAG TGGTACGGGA GTTTCCTGGG GTCTGTACCC

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+2  L A G H P F Q N E D Y R F R S A S P S F
4321 CTTAGCTCAG CACCCCTTCC AAAATGAGGA CTATCGTCCC CGGAGCGCCA GCCCCAGCCC
    GAATCGAGTC GTGGGGAAGG TTTTACTCCT GATAGCAGGG GCCTCGCGGT CGGGGTGCGC

-2  T H V L G G N Q W R T G P W G A C S S T
    TSP7
=====
4381 CACCCATGTG CTCGGTGGAA ACCAGTGGAG AACTGGCCCC TGGGGAGCAT GTTCCAGTAC
    GTGGGTACAC GAGCCACCTT TGGTCACCTC TTGACCGGGG ACCCCTCGTA CAAGGTCATG

+2  C A G G S Q R R V V V C Q D E N G Y T A
    TSP7
=====
4441 CTGTGCTGGC GGATCCCAGC GGCCTGTTGT TGTATGTCAG GATGAAAATG GATACACCCG
    GACACGACCG CCTAGGGTCG CCGCACAACA ACATACAGTC CTACTTTTAC CTATGTGGGC

+2  N D C V E R I K P D E Q R A C E S G P C
    TSP7
=====
4501 AAACGACTGT GTGGAGAGAA TAAAACCTGA TGAGCAAAGA GCCTGTGAAT CCGGCCCTTG
    TTTGCTGACA CACCTCTCTT ATTTTGGACT ACTCGTTTCT CGGACACTTA GGCCGGGAAC

+2  P Q W A Y G N W G E C T K L C G G G I R
    TSP7 TSP8
=====
4561 TCCTCAGTGG GCTTATGGCA ACTGGGGAGA GTGCACTAAG CTGTGTGGTG GAGGCATAAG
    AGGAGTCACC CGAATACCGT TGACCCCTCT CACGTGATTC GACACACCAC CTCCTGATTC

+2  T R L V V C Q R S N G E R F P D L S C E
    TSP8
=====
4621 AACCAAGACTG GTGGTCTGTC AGCGGTCCAA CGGTGAACGG TTTCCAGATT TGAGCTGTGA
    TTGTTCTGAC CACCAGACAG TCGCCAGGTT GCCACTTGCC AAAGGTCTAA ACTCGACACT

+2  I L D K P P D R E Q C N T H A C P H D A
    TSP8
=====
4681 AATTCTTGAT AAACCTCCCG ATCGTGAGCA GTGTAACACA CATGCTTGTC CACACGACGC
    TTAAGAACTA TTTGGAGGGC TAGCACTCGT CACATTGTGT GTACGAACAG GTGTGCTGCG

+2  A W S T G P W S S C S V S C G R G H K Q
    TSP9
=====
4741 TGCATGGAGT ACTGGCCCTT GGAGCTCGTG TTCTGTCTCT TGTGGTTCGAG GGCATAAACA
    ACGTACCTCA TGACCGGGAA CCTCGAGCAC AAGACAGAGA ACACCAGCTC CCGTATTTGT

+2  R N V Y C M A K D G S H L E S D Y C K H
    TSP9
=====
4801 ACGAAAATGTT TACTGCATGG CAAAAGATGG AAGCCATTTA GAAAGTGATT ACTGTAAGCA
    TGCTTTACAA ATGACGTACC GTTTTCTACC TTCGGTAAAT CTTTCACTAA TGACATTGCT

+2  L A K P H G H R K C R G G R C P K W K A
    TSP9 TSP10

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The following information is for informational purposes only.

5521 TCACCTTGAT GTCCTATTGG CATAAAGAAG AAATTATTAC AGGGGCTGCA AACTCATAGG
 AGTGGAACTA CAGGATAACC GTATTCTTC TTTAATAATG TCCCCGACGT TTGAGTATCC

 5581 ATGCTGTGAG GTGCCTGAAG ACAGTTAAGT ATAAGAAAAT ATTGTAGTGC CAGGGATACA
 TACGACACTC CACGGACTTC TGTCAATTCA TATTCTTTA TAACATCAGG GTCCTATGT

 5641 ACAAGGAGAG ATGGCAACTG TGACAACTA GCACATGCTG TGTGAAGGGA GCAGAATCTC
 TGTTCCTCTC TACCGTTGAC ACTGTTTGAT CGTGTACGAC ACACTTCCTT CGTCTTAGAG

 5701 ITTCACTCCA GCTGTGGCCA TGCAGAAATG TGGTCTAGCG TTACCAGACC TGATTTTTCA
 AAAGTGAGGT CGACACCGGT ACGTCTTAC ACCAGATCGC AATGGTCTGG ACTAAAAAGT

 5761 AGAGAGGCTA AAAATCTGGA CTAGTATGTG AGATTTCCTA ACTTGAAAAT GGGGGCTGAA
 TCTCTCCGAT TTTTAGACCT GATCATAAC TCTAAAGGAT TGAACTTTTA CCCCCGACTT

 5821 ATTTTGGTT TAAAAACATT GTAAGGGGCA AACAAACCCC TTTCATGAAC CAGATGTGTT
 TAAAAACCAA AATTTGTAA CATCCCCGT TTGTTGGGG AAAGTACTTG GTCTACACAA

 5881 GTGCCTGTTT AACAAACAGC TTCAGAGGAA GAAAATAATT TTCTATAATA TCCGAAGTAT
 CACGGACAAA TTGTTGTGCG AAGTCTCCTT CTTTTATTAA AAGATATTAT AGGCTTCATA

 5941 CTCAAGTACC ATTTTTTCAT ATATCTTCCT GTGCACAATG CTTATCTAGA CCCTTTTTAA
 GAGTTCATGG TAAAAAAGTA TATAGAAGGA CACGTGTTAC GAATAGATCT GGGAAAAAT

PolyA Site

=====

6001 TGGTAATAAA CCAGTAGTAA TCAT
 ACCATTATTT GGTCATCATT AGTA

The GENE database

Fig. 4

Metalloproteinase Domain Alignment of TS-SI v ADAMTS Family

						Percent Homology (SI vs)
						Ident
						Sim
301						
hADAMTS-4	(AB014588)	(212)	REFASLSREVTLLVADUKMAAFHG-AGLKRYLLIUMMAAAAARKHPFIRNPSLWV ³⁶⁰ TLV			46
hADAMTS-5	(AF142099)	(261)	RSISRRAROVLLLVADSMARLKG-RGLOHYLLIPLASIANRVSYSHAENHTRIAVVKV			44
hADAMTS-1	(AF060152)	(235)	REVSSHREVTLLVADQSMAEELG-SEKHRYLPLVPSAARFKHPFIRNPSLWVVKIL			50
hADAMTS-8	(AF060153)	(214)	REVSEAREVETLAVADSNPAFVG-ADIQNRLIPLVMSAARVYKHPFIRNPSLWVVKIL			62
hADAMTS-2	(AJ003125)	(260)	HAADDDYNVAVLGVDSVQETHEKEROKYLSLNNVNEVETKHDESGAHENVYVYVLI			49
nADAMTS-SI		(287)	RELISPREVEVAVENRMVSHG-ENIQHYLRELMVAVSMMKDPETIGNLNNVYVYVLI			33
Consensus		(301)	RF S REVETLLVAD SMA FHGK GLOHYLLIPLASIAARIYKHPSI N INLVVVK			
361						
hADAMTS-4	(AB014588)	(271)	MGSEGEQVQGP-SAAQVRSVAVRGLNTPEDSDP ⁴²⁰ HILFQDLGGVS-TGD			
hADAMTS-5	(AF142099)	(320)	VIEGDKKSIYVSK-NAAATLNFVKKHGHQOLGDDDEHYFA ⁴²⁰ EDGEGHH-SGD			
hADAMTS-1	(AF060152)	(294)	VHDEQKGEVDS-NAAALTIRNFNKKOHNPESDRDAEHY ⁴²⁰ ETLWTRQDGGSQ-TGD			
hADAMTS-8	(AF060153)	(273)	MEDEKQGEVSD-NALTRNFNRRFRQESDRPPEH ⁴²⁰ YATLWTRQDGGSQ-TGD			
hADAMTS-2	(AJ003125)	(320)	RESYGKMSLIEIGNPSQSENVRRAYLQKEDTGHDE ⁴²⁰ YHITWTRQDGGSQ-TGD			
nADAMTS-SI		(346)	VHNEQDQPSVFNAAQTNFVQSHKRSVGG--IH ⁴²⁰ ETWTRQDGGSQ-TGD			
Consensus		(361)	VL DE GPEVS GNA TLRNFC WQ N P D H EHYDTAILLTRQDLCC G CD			
421						
hADAMTS-4	(AB014588)	(329)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISLINGLST			
hADAMTS-5	(AF142099)	(378)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISETFGSTEDK			
hADAMTS-1	(AF060152)	(352)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISETFGSTEDK			
hADAMTS-8	(AF060153)	(332)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISETFGSTEDK			
hADAMTS-2	(AJ003125)	(376)	MOEYAPVTCGHEVRSQVNHDFSRVAVVAVH ⁴⁸⁰ TSHVIGNEHSGOGRGDEVRLGS--			
nADAMTS-SI		(402)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISETFGSTEDK			
Consensus		(421)	TLEMDVGTGDDARSDDDLQGLVAVL ⁴⁸⁰ LVFNMLN-SKPISETFGSTEDK			
481						
hADAMTS-4	(AB014588)	(388)	RHVAVVVAHVDPPEEPFARFVLE ⁵⁴⁰ DNGSHLQKLEA-PLHLRVTF--KDD			
hADAMTS-5	(AF142099)	(437)	-RVMSSITSDASKPKKQKATLDEFDDGHG ⁵⁴⁰ QVLDLARK-QILGDEEL--QTD			
hADAMTS-1	(AF060152)	(411)	HVMASMSNDHSQSPSPSAYMSTFDNGHGEINDKQON-RIQLGDLPS--TSD			
hADAMTS-8	(AF060153)	(391)	-HVMAPLVHLNQTLPSPSAMYTELDDGGHG ⁵⁴⁰ QVLDLARK-QILGDEEL--QTD			
hADAMTS-2	(AJ003125)	(434)	--HMAPLQAAFRRFHSRQOQESRRVHSH--YD ⁵⁴⁰ GLDDDFAHDWBALPOLPS--LHYS			
nADAMTS-SI		(460)	-HVMAPLVHLNQTLPSPSAMYTELDDGGHG ⁵⁴⁰ QVLDLARK-QILGDEEL--QTD			
Consensus		(481)	RHVMAP L D PWSPCS A ITEFLD GHG CLLD P ARP PLP LPGRM YD			
541						
600						

Percent Homology (SI vs)
Ident
Sim

FIG 5

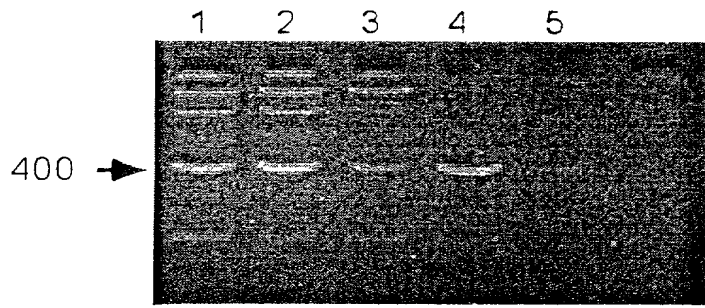
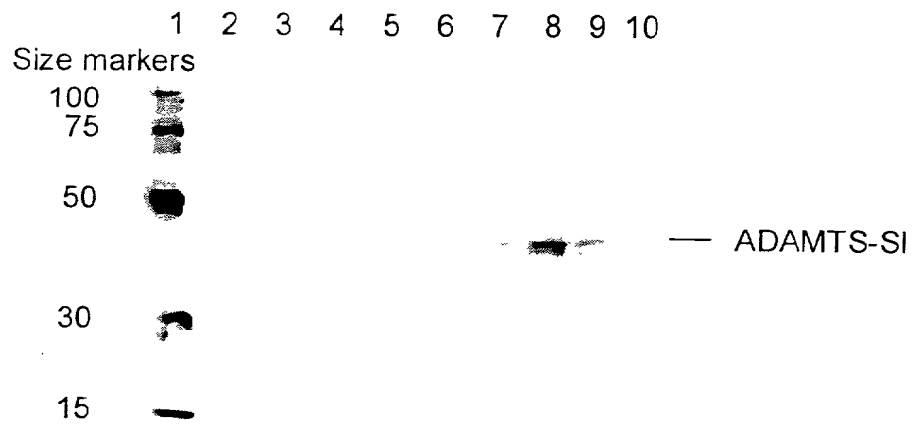


Figure 6



- Lane 1 His Ladder (Qiagen)
- Lane 2 Empty well
- Lane 3 Total lysate
- Lane 4 Unbound material
- Lane 5 Wash material
- Lane 6 50 mM Imidazole Eluate
- Lane 7 100 mM Imidazole Eluate
- Lane 8 250 mM Imidazole Eluate
- Lane 9 2nd 250 mM Imidazole Eluate
- Lane 10 Ni-NTA resin

FIG. 7

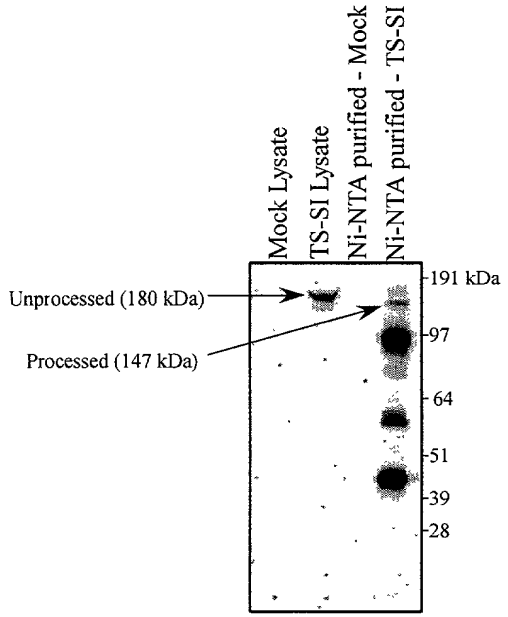


FIG. 8

A



B



Lane 1 2 3

1 2

Western Blot analysis of ADAMTS-4 and ADAMTS-SI cleavage of aggrecanase substrate. A, lane 1 = uncleaved substrate, lane 2 = ADAMTS-4, lane 3 = ADAMTS-4 + 1 μ M compound I. B, lane 1 = ADAMTS-SI and lane 2 = ADAMTS-SI + 1 μ M compound I.

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